

Theodor Meynert and Sigmund Freud; Dialog on the future of Psychiatry

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Author preface

In this fiction Theodor Meynert and his student Sigmund Freud are projected in time from the late 1800's to the present. They are updated with the current state-of-the art sciences of the brain, neurology and psychiatry and they meet in a café in Vienna to discuss the cutting edge of psychiatry circa 2011, and offer a fresh outlook for the future of the field.

Sigmund Freud has reached world fame and is well known, Meynert was his teacher and chair of the department where Freud studied and later trained as a resident. Many of the ideas developed by Freud were based on his learning from Meynert who was an authority and world leader in neurology and psychiatry of his time. In comparison to Freud's writings and theory, Meynert's work is to a great extent less known and surely not as popular as that of Freud. Concepts such as "Ego" that are typically attributed to Freud actually came from Meynert, and the general idea of a developing self organizing Ego can be traced back to the teachings of Meynert with regard to the developing brain (1). Meynert thought highly of Freud the student and resident, but became disappointed with Freud after the latter returned from Paris, taking, what seemed to Meynert and others, a non-scientific direction leading the field in the wrong direction, toward speculative psychology. Meynert was a strict professional and adhered to the empirical clinical science of the brain. He criticized the term 'Psychiatry' arguing for "disease of the for-brain" instead (1). In retrospect it seems to me we need Meynert today even more than he was needed in his era. With this short manuscript I will advance

Meynert in time to put forth his vision about the future of psychiatry. Freud as his student and influential figure will accompany him and may reconcile some of the divergence rooted in their pasts. This short paper portrays their presumed opinions on contemporary psychiatry in light of their original contributions.

Dialog Meynert Freud

Meynert - Good to see you Sigmund please have a seat; a strange thing seems to have happened to us - we have been catapulted through a time-machine to the future - this is the summer of 2011. I had time to get updated with the current developments in psychiatry and the neurosciences but I did not figure out why we are in 2011. The fact that you are the only one also traveling in time with me tells me that it has to do with our past contributions to humanity, and since they were professional in nature our trip is probably related to psychiatry.

Freud - Good to meet you too, the same thoughts crossed my mind as well and I reached similar conclusions

Meynert - Dear Freud have you had time to catch up and learn about the advances in our field, have you become aware of the incredible leap of technology that has transpired.

Freud - Yes, especially the internet - such availability of information, and flooding of information.

Meynert – Yes the internet allowed me to illuminate myself with the occurrences of our profession. You my dear Sigmund have been a major influence in the field. There is wealth of literature based on your work and I must say you were quite productive in the years following my death. My predictions about your abilities and talent were validated; it was such recognition that has driven me to offer you privileged work in

my laboratory. However I see that the unfavorable direction you took after returning from Paris has been maintained and even accentuated in your work, this seems to have important consequences on current conditions of the profession, and I must say my friend that many of these seem distasteful to me.

Freud - Yes I am fully aware of our divergent opinions from back then, you did not approve of my use of hypnosis and suggestive therapy (2) you thought hypnosis was pathological, inhibiting the cortex and thus liberating uninhibited psychotic-like sub-cortical activations that can harm and worsen patients' conditions. I later developed some of your ideas in ways that you obstinately objected. You insisted on objective empirical brain-related conceptualizations but the time back then was not ripe for such conceptualizations; we did not have the technology to advance these ideas.

Meynert – Is that a reason to go astray? Are we not empirical scientists?

Freud – I have always emphasized the need to go back to the brain; I argued that in the future my theoretical developments should become brain-related. I repeatedly declared that once advances in neuroscience allow, my ideas would become neuroscientific again.

Meynert - And has that occurred?

Freud – I must admit that if it has occurred it remains very limited and unsatisfactory. I will not hide my disappointment, especially as I see that the time is ripe for such psychological

neuroscientific unification, and still it has not happened. Especially frustrating is the fact that certain scientific associations such as "Neuropsychanalysis" have focused on this challenge, and have yet to fully achieve it. The gap-bridging-knowledge between our ideas and brain-based psychiatry has been developed to the full extent with Neural-Computation, Computational-Neuroscience and Neural-Network Modeling, and still they don't see it. Those claiming the goal of Neuropsychanalysis missed their objective by failing to use this knowledge in their scientific work.

And dear Theodor I will not hide from you my dissatisfaction with much that has been written about me and my ideas. Conceptualizations that are beyond me and that I would have totally opposed have been associated with me; I cannot hide my disappointment in being so extensively misunderstood. I have never meant for my clinical interpretations to become so malleable that they can be so readily adapted in such a way that an idea and its inverse are equally explainable. This posits the field in a very problematic irrational position where everything is plausible and at the same time inconceivable. I did not mean for that to be.

Meynert – So my stubborn insistence for an empirical physical psychiatry is of some value after all. But I must also confess dissatisfaction that my ideas did not seem to flourish historically. One example you mentioned is the term "Ego" and its original meaning. Very few know that when I first used the term "Ego", I originally intended to describe developmental brain organization in terms of neural networks, Your writings have turned it into a concept that is unrelated to the brain and open for endless interpretations and formulations none of which

can be validated empirically. I have read with pleasure that recently evidence for my "Ego" in the brain was revealed in what is called the "default-mode-network" (3, 4).

Freud - Yes I saw that, it was even linked directly to many of the conceptualizations that I later used to describe the Ego. It was published in the April 2010 issue of *Brain* (4) in a brilliant paper by Carhart-Harris and Friston, titled "The default-mode, ego-functions and free energy: a neurobiological account of Freudian ideas."

Yes, I see what you mean; it is my name in the title when you are the one that conceptualized "Ego" as network organization of the brain. Nevertheless your original concept of "Ego" as a basic individual neural network organization in the brain, could not have been validated back then. I have taken your idea and developed it theoretically, introducing it conceptually for use in the clinic. That is what made it so popular.

Meynert - Yes you have a point there, hopefully the development of computational neuroscience, that to my great pleasure offers the mathematics necessary to develop a network brain-related science for mental disorders, will eventually close the loop started with my ideas, via your theoretical contribution and back to my original thoughts. I was very happy to see some preliminary publications based on that concept (Peled 5, 6) and even a book titled "NeuroAnalysis" by Avi Peled (7). He emphasized this linkage and related it to personality disorders just as I would have done if I were to live and work in this millenium.

Freud – In relation to mental disorders, our work back then lacked a direct application to the clinic, you could not delineate a clear connection between brain disturbances and most of the more complicated mental disorders. I realized that in Paris, when I was writing about male hysteria (2). I realized that the story between patients' symptoms and brain function as we understood it then was much more complicated. Dynamics of thought, symbolism and experiences, biased upbringing and early distorted occurrences are all involved. I tried to explain these mental disorders using theoretical assumptions about how normal and pathological experiences and ideas may interact in health and disease. These ideas originated from my experiences with my patients and were developed to provide better understanding of the patient.

Meynert – Let's examine the attempt to reveal the causes of our patients' suffering. Today, there is a diagnostic book, titled DSM (Diagnostic and Statistical Manual) that classifies mental disorders according to the patient's complaints (symptoms) and clinician observation (signs). This descriptive nosology does not relate to the origins of the disorders. Unlike other fields of medicine where the taxonomy reflects the etiology (causes of the disorder), for example "appendicitis," refers to a body part and its morbidity. Current taxonomy for mental disorders such as "Depression" and "Anxiety" does not correspond to body parts or to any impairments or changes in any given body parts.. These are just plain descriptions that do not provide any information as to what may have gone awry in the brains of patients suffering from mental disorders.

The DSM seems to have been an outgrowth of a crisis that took place in the seventies of the previous century, and that crisis can indeed be attributed to a great extent to your work, my dear Freud. After your visit to America psychoanalysis became very popular with the American Medical establishment. This made psychiatric practice in America very different from that of Europe, and this allowed for a famous US UK cross national study in 1975 to argue how unreliable psychiatric diagnosis is. At the same time another famous paper titled "Being sane in insane places (8)" by Rosenhan in 1973 showed that reliance on American psychiatric practice hardly distinguishes normal's from mentally ill individuals. These findings almost gave a mortal blow to American psychiatry which at that time began to be synonymous with world psychiatry. In an effort to save the face of psychiatry the DSM approach was adopted, one that totally excludes any etiological assumption about the causes of mental disorders. The trauma of a non reliable psychiatry created a consensual, thus more reliable psychiatry but one that cannot be validated as it is based on taxonomy that is not related to the nervous system.

Freud – I agree that things seem dim for the field; I would have expected that by now my psychological ideas would have already merged with neuroscience. My initial ideas that Ego formation develops gradually based on experiences, i.e., it is shaped by reality, upbringing and interactions with the primary care givers, and lends naturally to the modern findings of experience-dependent-plasticity and are readily connected back to the brain organization via Hebbian dynamics. Donald Hebb (9) formulated the mechanisms by which neurons interact (strengthen) with connections in order to store information, create memories and thus offer an internal representation of the

world in each individual. This internal representation of the outer world includes the complicated psychosocial world of relationships and also the internal representation of one's self.

I have seen that those who came after me and wanted to continue my line of thought developed what they called "object relations psychology" concentrating on the internal representations and their dynamic, maturity and integrity. They showed how people use these internal representations and perceptual maps to determine both how they experience the outer world of psychosocial occurrences, as well as how they experience themselves in that context. This, off course, creates the context which guides their reactions and psychosocial behaviors and defines their personality traits.

And my dear Meynert this conceptualization even though unrelated to the brain has helped clinicians understand personality disorders. This type of conceptualization proposed the description and definition of personality disorders in terms of immature, biased, split internal representations. Furthermore in therapy, once the clinician has diagnosed (psychodynamic diagnosis) the disturbances of internal representations he could foresee and treat the disturbances and biases in the patient's experience of things, and thus his reactions and consequent behavioral patterns.

In light of my original quest for a scientific psychology, i.e., in current terms unified neuroscientific-psychology, one should view psychotherapy as an experience-dependent therapy in which Hebbian algorithms are put to work to create new organizations in the brain. As these new organizations are dependent on experience the therapeutic sessions should have a

corrective/altering manifestation that psychologists have wisely called "corrective experience."

Meynert - My dear Freud I have learned about a whole new field of science that has evolved after our time, a field of science that I am sure you would have been very pleased to base on your letters to Fliess, which as you have probably noticed, were found and published under the title of "the Project" (10). This new field is called computational neuroscience as described in the book titled "Parallel Distributed Processing" (11) published in the nineteen eighties that has become a classic in that area of knowledge. The book describes how information can be embedded in neural network models and provides a good explanation of how the real brain obtains the ability to store and maintain internal representations of the sort we have been talking about right now.

I emphasize this because my original idea of the Ego as a network formation in the brain, concords perfectly with developments of your followers who espouse "Object Relations" psychology. The Default Mode Network has been recently discovered by our colleagues - in 2011. Personality disorders can now be conceptualized as disorders of the Default Mode Network. In personality disordered patients the Default Mode Network is either undeveloped with rudimental, split poor internal representations causing them to experience biased inflexible, limited split experiences, or alternatively, developed but with biased experience-dependant internal constructs, which naturally cause non-adaptive ineffective performance and debilitating/impaired interpersonal relationships.

Freud – Yes I agree you have formulated it quite well.

Meynert – Dear Sigmund, I must tell you that I have found the book about "Parallel Distributed Processing" and the related neural-computation science that developed in this direction extremely interesting. I think the knowledge acquired using neural network models provides deep understanding of brain phenomena that we could have only dreamed about in our era. I am talking about higher-level general brain phenomena such as consciousness. Here I must confess that you had a great deal of courage to write about this subject early on, and your speculations led you to a fairly good model of conscious and unconscious processes. Off course, I would have objected to such wild speculations, and still think they had no serious scientific basis back in our time. Let me try to explain what I mean my dear Sigmund, because these ideas are also related to more physical aspects of the brain, i.e. complex systems.

In my readings I became especially interested in the developing knowledge of complex systems. Naturally the brain is a complex system and any psychiatrist who is not an expert in the sciences of complex systems does not merit the title of a professional in this field. Herbert Simon (1962) described complex systems as an organization which is 1) balanced between randomness and order and 2) hierarchically nested. Such systems are dynamically non-linear meaning that they do not have cause and effect relationships, and in addition they demonstrate "Emergent Properties" i.e., the whole is more than the sum of parts. Applying this to the brain, balanced between randomness and order relates to balanced connectivity versus disconnectivity and offers the equilibrium between randomness and order. As for hierarchically nested organization, unimodal primary processing brain systems combine to higher-level

multimodal processing systems until the brain organization culminates in global transmodal integration (12).

Consistent with the definition that the whole is greater than the sum of its parts, one neuron or even groups of neurons do not have psychological characteristics such as mood, awareness and consciousness. However the entire brain as a complex, dynamic equilibrated and hierarchical system has all of those features. Bernard Baars (13) elegantly described this in his "global workspace" theory. Partial processes that are parallel and independent, continually and flexibly combine to form global processes from which the content of conscious experience emerges as an Emergent Property. Only processes that contribute to the global process are conscious while all the processes that are "about to enter" or have "dropped out" of the global process are unconscious. Partial processes become conscious by participating in the overall transmodal brain organization.

Freud – my dear teacher, this knowledge has not escaped my readings, and you are correct, I was excited to find that my ideas about conscious, unconscious and subconscious could be mapped so well on a functional-anatomical brain structure. The partial processes are unconscious and those about to enter and become conscious are subconscious processes. Whenever a partial process is excluded from the global organization it fits my theorization about repression, being excluded from global processes the pretrial process is actually repressed into the unconscious level of brain organization. In effect all the defense mechanisms that I have conceptualized and were later developed by my daughter Anna fit perfectly into this model presented by Bernard Baars. For example if we view the global

organization as a network of interrelated and constrained processes, then the global organization will determine which processes will participate in the global message. For example if the content of a process contradicts the global message, i.e., conflicts according to my old terminology, then it will either become repressed or will need to change or even inverse its content. For example in reaction-formation unconscious contents inverse in order to be able to fit the general message and participate in the general organization. My dear Meynert, I can see how delighted you are that my speculations that were unrelated to the brain have become brain-related, they allow for your critical empirical physical approach to accept them.

Meynert - My dear Freud it is not for naught that I have been strict on this issue. If we ever want to intervene effectively with a brain-related treatment, we must have a brain-related knowledge of everything that has to do with mental functions and dysfunctions. In this respect it must be emphasized that Baar's description brings us closer to the brain but the formulations of Dehaene and colleagues from 2003 (14) finally touch the tarmac by mapping it in neural network formulations.

My dear Sigmund my student, can you see now that fortunately your speculations kept close to the intuitions you learned from me about the functioning brain, so as years progress your ideas still concord with the more advanced knowledge acquired in modern neuroscience. Your ideas of the unconscious and defense mechanisms still apply in modern neuroscience just as you initially intended them to.

Freud – Returning to the big picture they are also in agreement with the notion of Ego as a network structure with its internal

representations relevant for conscious experience. I still remember how you taught us about the Ego being formed from embedded pictures of experience. I cannot escape awareness of the historical injustice inflicted on you in this regard. In our time it was a well known fact that the conceptualization of Ego belonged to you, who would have thought it will not go down in history?

Meynert - I have searched the literature and found that my descriptions of psychosis as a weakening of connections among neuronal constructs have had a better fate. As you remember I argued that thoughts are represented by activations of groups of neurons and that associations correlate with connections among neuronal activations. I argued that in sleep and toxic conditions these connections can become weak resulting in the fragmentation of thought processes. Now that consciousness is involved with these structures it explains how the psychotic fragmented conscious experience comes about. If neuronal activations become statistically independent then no wonder that loosening of associations ensue. If the unimodal processes of speech recognition and interpretation become statistically independent, and thus unrelated to other brain activities such as visual perception, no wonder that voices coming from nowhere are experienced.

Freud – Yes and such disconnectivity and weakening of constraints must surely also involve the hierarchal formation of the complex brain. We must consider that such hierarchy offers also a top-down bottom-up balance where incoming signal travel up the hierarchy integrate and form higher level sensations which hold the content of perceptual consciousness upon which action is planned and executed. Marcel Mesulam in

his overview from 1998 (12) describes quite clearly how higher mental functions such as volition and motivation emerge from these highest levels of sensory-motor transformations. The disturbance of hierarchal balance can result in bottom-up insufficiency where the hierarchy fails to achieve higher-level organization or it can result in a top-down excess where the higher-level schemata constrain, and even bias, incoming information and sensations traveling up the hierarchy. With bottom-up insufficiency we can expect disturbed motivation and related activity; with top-down excess we can expect rigid, prejudiced-ideation to bias experience. When this deviation becomes incompatible with occurring events it achieves a delusional manifestation.

The four major disturbances can manifest concomitantly "disconnection," "over-connections," "top-down" and "bottom-up disturbances" create the spectrum of disturbances that we find in schizophrenia spectrum disorders. Notable disconnections disturb associations that in turn build the logical causality, thus disturbed logic contributes to erroneous experience and interpretations, resulting in delusional thinking. Overconnectivity may reduce the number of neuronal activation patterns by restricting interconnected activity, the number of activation patterns reduces, and the overly constrained interactions tend to activate the same neuronal ensembles resulting in repetitive restricted ideation such as that of perseverations and poverty schizophrenia.

Meynert - Yes dear Freud, 2011 science offers a brain-related formulation for schizophrenia that is consistent with my initial formulation. In effect this is clearly described in a monograph titled "Neuroanalysis," (2008) that I found very interesting as it

is about brain-related psychiatry and in accord with my view of things. This monograph did not use the non-scientific term of "psych" from your term of "Psychoanalysis." As you know my dear Freud, in my mind substituting "Neuro" for "Psych" seems to be the correct "next" step.

Freud – Based on our conversation so far, we have offered a brain-related conceptualization for personality disorders and psychotic schizophrenia spectrum disorders. This covers a large portion of psychiatry, but what about mood and anxiety disorders? I have formulated anxiety as resulting from threatening content, or activity, risking destabilization of Ego-formation. How do you think this can reconcile with what we know in 2011?

Meynert - I think the knowledge accumulated so far until 2011 can offer a solution to that question, however we must take a step back and first determine how the brain generates mood. Let us look at the big picture first. Let's agree that mood is an emergent property of brain organization, as such it must involve wide-spread whole-brain dynamics. Now let's focus on mood related processes that are relevant to distributed whole-brain activity. Nowadays clinicians know that antidepressant activity related to SSRI (serotonin specific reuptake inhibitors) effects approximately 60% of the cortical neurons, and that it is synaptogenetic, i.e., it increases neuronal resilience and plasticity (15). We can thus deduce that increasing whole brain plasticity and flexibility has an antidepressant effect, in other words an elevation of mood. It has also been established that depression is associated with neuronal death and reduced neuronal resilience due to reduced spines and dendrytici arborization (15). Thus we can presume that widespread

flexibility and adaptability correlate with elevated mood while the opposite dynamics, reduced flexibility and adaptability correlate with depressed mood.

Freud – I see what you are getting at. The brain continuously adapts its connectivity formations to environmental external stimuli (16). Actually, as we have determined earlier, it encodes the environmental occurrences creating internal representations of the environment via Hebbian synaptic plasticity and dynamics (7). There is a continuous match between the external occurrences and the internal representations. Adaptability in this sense is achieved by the brain's ability to continuously reduce the "differences" or "biases" between internal representations and external occurrences (4). This is also represented in the free-energy principle of Karl Friston's work, and also concords with my ideas of a "developing Ego" via reduction of drives (17).

If I elaborate further on your idea about whole brain dynamics of mood and anxiety then we can assume that in order for the brain to adapt to incoming information and to create a good adaptable matching between internal representations and external occurrences, it should achieve levels of flexibility equal to those of environmental occurrences and their dynamic changes. Taking this line of thought to the next level we can begin to view the interacting brain-environment using the concept of "Optimization". In this case optimization will be defined as the extent to which the outer world is optimized within internal representations. Accordingly if the brain is flexible enough to match the ever changing environmental occurrences, it maintains a good matched internal representation of the world. If however the brain is not flexible

enough and the pace of environmental changes outruns the adaptability of the nonflexible brain then a bias may ensue and the internal representations will not match the environmental occurrences, or in other words the internal representations will not be optimized, and in terms of system physics this can be denominated as de-optimization dynamics.

Meynert - Excellent formulation my dear Sigmund, now you have brought this to the next level. We can now assume that optimization of internal representations involve good matching dynamics, which in turn depend on plasticity of synaptic-dynamics and relates to mood. Optimization dynamics emerges as elevation of mood while de-optimization dynamics emerges as depressed mood. This explains why antidepressant medications work, they are synaptogenic and they increase flexibility allowing for better matching dynamics thus triggering optimization dynamics emerging as elevation of mood. Contrarily, anything that reduces brain plasticity and flexibility will trigger mismatched dynamics between internal representations and external occurrences. Such mismatched dynamics will result in de-optimization dynamics emerging as depression.

Freud – Now it becomes clear how stress generates depressed mood. Stressors always entail drastic abrupt changes in the environment thus altered shifted experiences or oscillations, if you will, of incoming stimuli. The task for the brain is to outmatch such abrupt oscillatory changers and for that it must be flexible, malleable enough. Stress with its abrupt changes challenges brain flexibility and adaptability. If the brain is not flexible to the extent that the challenging stress dictates, internal representations will not be able to match the changes

originating from the stressful event, de-optimization dynamics ensues and depressed mood is experienced. This is the mechanism of reactive depression.

Meynert - The other side of the coin relates to depression encountered in various medical conditions and old age. As we know depression is very common in demented elderly patients. Medical conditions that hamper neuronal resilience, especially old age with dementia where neural cell death is documented, reduce brain flexibility. In turn the degree of change that an inflexible brain can counter is also reduced. The phenomena where elderly patients become depressed due to minor changes in their environment are well known. Transfer of a demented elderly patient to a geriatric care facility typically triggers depression. So the term of endogenic depression can be reformulated as hampered brain flexibility to the extent that even regular (non-stressful) dynamics of the environment are hard to counter and to adapt to, resulting in gradual progressive de-optimization dynamics.

Freud – we cannot ignore the explanation for "Anxiety". In my theories it plays a major role in many mental disturbances and I have hypothesized that it results from unconscious contents threatening Ego-integration. How do we reconcile that with what is known today?

Meynert - Anxiety is a very general symptom generated during many of the mental disorders thus it should be viewed as associated with the general stabilization dynamics of neural networks in the brain. At the same time it should also be viewed as a whole-brain-disturbance because like mood it is an emergent property. Neural networks have basic innate

characteristics of "multiple constraint dynamics. (6,7)" In other words every neuron is constrained by the input it gets from multiple other neurons connected to it. Multiple constraints mean that the value the neuron assumes is determined and constrained by all the other neurons connected to it. Such constraint satisfaction dynamics is spread in the network and constantly changes as the network performs its computational tasks. The constraints keep the network activity integrated, but the changes imposed on the network during computations may strain the constraints and tend to disrupt them. For example if constraints on a neuron change very rapidly and the value of the activity of that neuron did not have the time lapse needed to conform with the altered constraints, then the values of the activity of the neuron will not "comply" with the constraint and this may destabilize the organization of neuronal activity. In a network such disturbances are dispersed over many connections and are thus absorbed by the structure of the network. Nevertheless if the destabilization is strong enough it can spread in the network risking destabilizing the global organization of the network. Such a destabilization spread in the network is expressed as an emergent property of Anxiety.

Freud – I see what you are getting at, if the Ego is a network structure it is obvious that any type of dynamics that frustrates the constraints in its network structure will be experienced as an anxious sensation. Regular computations frustrate constraint all the time as an ongoing regular process, so some basic level of anxiety is always there. In addition, any stressful event that challenges the matching dynamics we have just discussed will result in concomitant "strains" on network connectivity; this is a good explanation for the anxious sensation accompanying stressful events.

As for my theories of defense mechanisms, now that we are aware that defense mechanisms are actually related to the dynamics of partial processes and their participation in global processes that make up the content of consciousness, then my ideas of anxiety that are related to unwanted contents introduced into conscious awareness are beginning have their brain-related explanation. Any partial process that is incompatible with the global message of transmodal brain organization will tend to "strain" and disrupt the network of the global organization. Being incompatible means that the network partial-process-activation applied to the global organization is incompatible or in other words, unfit for the network constraints and thus "frustrate" and "strain" the organization. Thus incompatible unfit messages trying to get access to the general conscious message destabilize the global network activity resulting in the emergence of anxious sensations. So my theorizing of anxiety emerging from unconscious threatening impulses has a biological neuroscientific explanation with this model.

Meynert - Yes my dear Freud these brain-related scientific facts also explain why most if not all mental disorders are accompanied by some level of anxiety, because all mental disorders have to do with one or another level of network destabilization. Moreover, our experience shows that patients suffering from mental disorders typically complain of depression and anxiety. Their depression is typically ongoing continuous life-spanning with exacerbations during stressful events that are due to inflexible non-adaptive behaviors. We have previously determined that Personality Disorders involve immature biased non-adaptive internal representations related

to similarly altered, immature biased neural-network configurations. Typically such internal representations are biased from the actual occurrences of real-time environmental events. As a result there is a certain degree of ongoing continuous mismatch between the internal representations and external occurrences. We have already established that such a mismatch causes the emergent property of depressed mood; this offers an explanation as to why patients suffering from personality disorders typically feel depressed for most of the time.

Freud – Dear Meynert during the short time of our conversation we have utilized the available science of complex-systems and computational neuroscience and have understood Consciousness and Mood as emergent properties arising from complex systems physics. We understood Personality in the form of internal configurations and default mode Ego networks; we deciphered how Defense Mechanisms work within the dynamics of partial versus global network whole-brain organizations. We also understood that such constructs can become fragmented, disconnected, and disturbing hierarchical brain organization, thus disrupting coherent stable experiences causing Delusions and Hallucinations generating the clinical phenomena of Psychoses and Schizophrenias. We elaborated on how brain plasticity, environmental changes, i.e., stressors and non-adaptive biased internal representations play important roles in causing the emergence of different types of depressions. We also understood Anxiety as a sensation emerging from general distributed neural network destabilizations in the brain. Don't you think my dear Meynert that the psychiatric professionals of 2011 have most, if not all,

they need to re-conceptualize mental disorders as brain disorders?

Meynert - Yes my dear Sigmund you are correct. Personality Disorders can be reconceptualized as disturbances to the default mode network. These can be of network structure development or any other organization parameter that is altered compared to the mature optimal networks of those that do not have personality disorders. Psychosis and schizophrenia can be readily reconceptualized as disturbances to fast millisecond-range connectivity and hierarchical dynamics. Finally Mood and Anxiety disorders are emergent properties from disturbances of optimization and constraint-frustration of slow and fast plasticity dynamics, respectively. Special cases such as Obsessive Compulsive Disorder fall into specific dynamics such as that of repetitive activations when over-connectivity of certain neural ensembles cause them to repeatedly reactivate themselves. This can happen in certain cases of repetitive experiencing of trauma, for example in certain clinical manifestations such as post-traumatic syndromes.

Freud – But my dear Meynert why haven't 2011 professionals achieved such readily available conceptualizations? Why are they caught up with their descriptive, subjective non-validated diagnostic system that they call DSM?

Meynert - I am afraid my dear Freud that you yourself have contributed to this state of events. Your contribution is probably partial and indirect, but it is relevant to the DSM. In the beginning of our discussion we mentioned what occurred in the nineteen seventies which has lead to the establishment of the DSM III, the US UK and the Rosenhan studies. Until that

time American psychiatry was typically dominated by psychoanalytic practice and diagnosis, and that was unreliable as there were no consensual formulations and practices. Specifically it was in contrast with European psychiatry which was not psychoanalytic and was based on descriptive phenomenology. The fact that psychiatrists diagnosed patients according to different conceptualizations revealed the total lack of reliability in psychiatric diagnosis. The crises that ensued with the revelation of such unreliable diagnosis triggered the efforts for a consensual psychiatry that would achieve reliability based on consensus. I am afraid my dear Freud that clinging to the DSM even today results from the trauma that psychiatry endured in the seventies. Today, psychiatrists are still afraid of any new conceptualization that might cause similar reliability problems to psychiatry.

Freud –I did not mean for that to happen. My dear Meynert what do you think should be done in order to correct this state of affairs?

Meynert - They will need proof, validation for the novel brain related conceptualization of mental disorders that we have just formulated. Actually, the first signs of disillusion from the DSM approach are evident, a new project of the NIMH, the American National Institute of Mental Health, titled the Research Domain Criteria (RDoC), is directing research funds to brain related research of mental disorders. They have decided to abandon the DSM criteria as a research guide and use more general phenomenological domains such as "negative" and "positive" valence systems. For example, negative valence includes fear, stress and aggression, and "cognitive systems" such as attention, perception and working

memory. Each of these domains plan to have research ranging from genetic molecular levels up to whole-brain levels and even social (external brain) levels (18). The only advancement they achieve in my mind is the acknowledgment that the neural network intermediate level has a significant explanatory level of description. Being in an intermediate level it is positioned with good explanatory power going up the hierarchy to whole-brain level and down the hierarchy structure to the molecular level. However having taken this important step they fail to take the next obvious step and use neural network sciences, that we have just applied, to focus their efforts. They have chosen to stay on a general level assuming the big picture will bring the solution for brain related psychiatry. I tell you my dear Freud that they are mistaken, if their objective will be accomplished it will only be after centuries of research. In order to reach the goal of neuroscientific psychiatry faster they must take the bold step and put into practice what we have just discussed. They should use complex neural network sciences to formulate the theory necessary for neuroscientific psychiatry. If they adapt our conceptualizations they will narrow down the effort and have a brain-based diagnostic system within decades instead of centuries. In my search of the web I have encountered an unknown book and project titled "NeuroAnalysis (7)" which actually follows our insights from this conversation. NeuroAnalysis proposes a Clinical Brain Profiling (CBP) procedure that translates clinical descriptive phenomenology into brain-related conceptualizations. It does so along the very similar lines of our discussion so far. It offers a redefinition of descriptive, phenomenology-based types of mental disorders as brain-related disturbances. In my mind it offers a better option than the RDoC. Even-though it is obviously preliminary in

nature, it readily offers a more focused and rationally-based approach.

Freud – My dear Meynert how will you convince them to take the path we have been elaborating upon just now? We must admit that most of our talk, as well as the NeuroAnalytic approach, is currently theoretical.

Meynert - Yes you are correct, but searching the literature you can find support and even an initial validation for our assumptions. Let us begin with the disturbances to the fast millisecond range connectivity and hierarchy-related organizations that we have assumed will correlate with psychotic schizophrenia spectrum disorders. There is a large body of data on this to the extent that reviews are beginning to emerge in the literature, for example, Jones writes about "Errant ensembles: dysfunctional neuronal network dynamics in schizophrenia (19)". Bassett and colleagues (20) wrote a paper titled "Hierarchical organization of human cortical networks in health and schizophrenia." It was published in the 2008 September issue of the journal *Neuroscience* and is really relevant to the ideas we were formulating about disturbances of hierarchical balance. There are also initial publications related to basic network organization the default mode network (DMN) and that correlate with the concept of Ego, Carhart-Harris and Friston wrote about it in their paper titled "The default-mode, ego-functions and free-energy: a neurobiological account of Freudian ideas (4)." It was published in *Brain* last year in 2010, and as you can see from their title it is based on your writings. Disturbances to the slow plasticity dynamics, those which transpire within a range of weeks and which optimize and adapt brain network organization to environmental occurrences. Such

disturbances have not yet achieved direct validation. I predict because of the concept of optimization which is currently hard to measure, however indirect findings to plasticity disturbances of learning in depression do exist. Nissen and colleagues published a paper titled "Learning as a model for neural plasticity in major depression " in last year's Biological Psychiatry journal (21). They show that reduced plasticity correlated with depression. As for connectivity disturbances in depression there is also a paper by Cullen and his group titled "Altered white matter microstructure in adolescents with major depression: a preliminary study (22)." These are, of course, only few examples and I am sure that a thorough literature search will find many more such examples.

Freud – My dear Meynert as promising as these papers are, I still find that they fail to convince and bring about the novel approach we were formulating today. This is probably also a good reason for the survival of the DSM.

Meynert - Yes my dear Sigmund I have to admit that one major obstacle is poised between a brain-based psychiatry and the current state of psychiatric science. This obstacle can be defined by the missing knowledge in the field of signal processing. The science of signal processing that can effectively process electrical and metabolic signals from the brain is rapidly progressing but has not yet reached the required effectiveness needed for definitive effective deciphering of brain algorithmic functioning.

A promising direction is that of "graph theory". This offers a mathematical formulation of network organization. One important discovery made using graph theory is that optimal

effective network systems are "Small World Networks." Having high clustering and short path length, small worldiness can be quantified via measurements such as "degrees," i.e., number of connections, for "Hubs," i.e., junctions of multiple connections, as well as by other additional parameters. Graph theory (23) readily lends itself to neural network oriented interpretations of brain signals. There are also advances in interpreting connectivity via signal processing, for example older assumptions of "coherence" and "correlations" are substituted by more complex "attractor domain" estimations and more advanced "Bayesian statistical" applications such as the "DCM" (dynamic causal modeling). But even though 2011 neuroscience of signal processing is advancing fast it still has some way to go to become a definitive critical factor that will revolutionize psychiatry.

Freud – We are first of all concerned about our patients and I ask myself how the progress we were delineating here will help the patients directly.

Meynert - Can't you see my dear Sigmund, once the algorithms of brain disturbances underlying mental disorders are revealed, the field will function somewhat on lines of the metaphor of cardiology. Cardiac arrhythmias causing cardiac insufficiency are corrected via cardiac pacemakers that eliminate the arrhythmias and restore cardiac function. Along the general assumption that mental disorders are brain-insufficiencies arising from sets of brain disturbances, or arrhythmias, if you will, then interventions of "brain pacing," or "brain pacemakers," will correct the disturbances, optimize brain functions and eliminate the symptoms and signs of mental disorders.

My dear Freud you have probably noticed to what extent technology has advanced in the year 2011. In my mind one of the most promising technologies recently being studied is that of "Optogenetics (24)". It offers the possibility to control neuronal activity and is directed to single cells and cell groups with the highest precision. This will probably become one of the leading technologies for the future "brain-pacemakers."

Additionally dear Sigmund, the medications that are synaptogenetic, such as the selective serotonin reuptake inhibitors, if they were to be developed further they may offer the possibility to make the brain more plastic. They may even achieve plasticity levels such as those occurring in brains of infants and children. You must surely see the potential of reshaping the brains of patients if they can reach such plasticity levels. Even by using experience-dependent- plasticity techniques of which psychotherapy, inspired by your work, is one. Other experience-dependent- plasticity therapies can be induced by multimedia computer technology available today, such as creating therapeutic experiences with virtual reality (25) or virtual-reality experience dependent plasticity if you will.

Freud – Yes I see the potential, combining plasticity induction, with both external experience -dependent-therapies as well as direct internally directed brain pacing will offer unlimited strategies to re-optimizing brain functions and curing patients.

Meynert - Imagine my dear Sigmund; psychiatry will finally become a medical scientific discipline. Hopefully my suggestion to abandon the disturbing un-scientific term of

"Psychiatry" will be accepted. Instead of the term "Psychiatry" we can use a brain-related terminology for example "NeuroAnalysis (7)" and "Clinical Brain Profiling (6)." The future psychiatrist, or "NeuroAnalyst" if you will, - will master medical science, neuroscience, complex-systems-physics, non-linear mathematics and signal processing knowledge. He will be the most advanced professional in the field of medicine as is suitable for a profession dealing with the most complicated and challenging organ in the body, the brain. The one organ that is responsible for us being human, and probably the highest level of creation in this world of ours.

Freud – Yes I totally agree with you dear Meynert

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